

WHAT IS CLAIMED IS:

1. A method of altering an insulin-associated parameter in a subject, said method comprising administering to said subject a ghrelin or analog thereof; and an unacylated
5 ghrelin or analog thereof.
2. The method of claim 1, wherein said method comprises administering to said subject a composition comprising a ghrelin or analog thereof; and an unacylated ghrelin or analog thereof.
- 10 3. The method of claim 2 wherein said composition further comprises a pharmaceutically acceptable carrier.
4. The method of claim 1, wherein said insulin-associated parameter is selected from the group consisting of:
 - (a) insulin level;
 - 15 (b) insulin resistance;
 - (c) free fatty acid level;
 - (d) insulin activity;
 - (e) insulin sensitivity; and
 - (f) any combination of (a) to (e).
- 20 5. The method of claim 1, wherein said alteration of an insulin-associated parameter is selected from the group consisting of:
 - (a) a decrease in insulin level;
 - (b) a decrease in insulin resistance;
 - 25 (c) a decrease in free fatty acid level; and

(d) any combination of (a) to (c).

6. The method of claim 1, wherein said method is for preventing or treating an insulin-associated condition.

7. The method of claim 4, wherein said insulin-associated
5 parameter is insulin resistance.

8. The method of claim 7, wherein said insulin resistance is associated with a state or condition selected from the group consisting of:

(a) postprandial state;

10 (b) reduced growth hormone level;

(c) reduced growth hormone activity;

(d) obesity;

(e) diabetes;

(f) intravenous nutrition due to critical illness;

15 (g) metabolic syndrome X; and

(h) any combination of (a) to (g).

9. The method of claim 8, wherein said state or condition is reduced growth hormone level, activity, or both.

10. The method of claim 9, wherein said reduced growth hormone
20 level, activity, or both are associated with a condition selected from the group consisting of:

(a) obesity;

(b) aging;

(c) pituitary gland deficiency;

(d) intravenous nutrition; and

(e) any combination of (a) to (d).

11. The method of claim 8, wherein said state or condition is diabetes.

5 12. The method of claim 11, wherein said diabetes is selected from the group consisting of type I diabetes and type II diabetes.

13. The method of claim 12, wherein said diabetes is type I diabetes.

10 14. The method of claim 13, said method is for preventing or treating the dawn phenomenon.

15. The method of claim 1, wherein said administration of said ghrelin or analog thereof and said unacetylated ghrelin or analog thereof is sequential.

15 16. The method of claim 1, wherein said administration of said ghrelin or analog thereof and said unacetylated ghrelin or analog thereof is simultaneous.

20 17. The method of claim 1, wherein said ghrelin comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 1 and a fragment thereof.

18. The method of claim 17, wherein said ghrelin comprises a peptide having the amino acid sequence of SEQ ID NO: 1.

25 19. The method of claim 1, wherein said unacylated ghrelin comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 2 and a fragment thereof.

20. The method of claim 19, wherein said unacylated ghrelin comprises a peptide having the amino acid sequence of SEQ ID NO: 2.

21. The method of claim 1, wherein said analog of ghrelin
5 comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 3 and a fragment thereof.

22. The method of claim 21, wherein said analog of ghrelin
10 comprises a peptide having the amino acid sequence of SEQ ID NO: 3.

23. The method of claim 1, wherein said analog of unacylated ghrelin comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 4 and a fragment thereof.

15 24. The method of claim 23, wherein said analog of unacylated ghrelin comprises a peptide having the amino acid sequence of SEQ ID NO: 4.

25. The method of claim 1, wherein said ghrelin or analog thereof and said unacylated ghrelin or analog thereof is
20 administered through a route selected from the group consisting of intravenous, oral, transdermal, subcutaneous, mucosal, intramuscular, intranasal, intrapulmonary, parenteral, intrarectal and topical.

26. The method of claim 1, wherein said ghrelin or analog
25 thereof is administered at a dose of about 1 µg/kg.

27. The method of claim 1, wherein said unacetylated ghrelin or analog thereof is administered at a dose of about 1 µg/kg.

28. The method of claim 1, wherein said subject is a mammal.

29. The method of claim 1, wherein said subject is human.

30. A composition comprising a ghrelin or analog thereof and an unacylated ghrelin or analog thereof.

5 31. The composition of claim 30, said composition further comprising a pharmaceutically acceptable carrier.

32. The composition of claim 30, wherein said ghrelin comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 1 and a fragment thereof.

33. The composition of claim 32, wherein said ghrelin comprises a peptide having the amino acid sequence of SEQ ID NO: 1.

15 34. The composition of claim 30, wherein said unacylated ghrelin comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 2 and a fragment thereof.

20 35. The composition of claim 34, wherein said unacylated ghrelin comprises a peptide having the amino acid sequence of SEQ ID NO: 2.

36. The composition of claim 30, wherein said analog of ghrelin comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 3 and a fragment thereof.

25 37. The composition of claim 36, wherein said analog of ghrelin comprises a peptide having the amino acid sequence of SEQ ID NO: 3.

38. The composition of claim 30, wherein said analog of unacylated ghrelin comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 4 and a fragment thereof.

5 39. The composition of claim 38, wherein said analog of unacylated ghrelin comprises a peptide having the amino acid sequence of SEQ ID NO: 4.

40. The composition of claim 30, wherein said composition is adapted for administration by a route selected from the
10 group consisting of intravenous, oral, transdermal, subcutaneous, mucosal, intramuscular, intranasal, intrapulmonary, parenteral, intrarectal and topical.

41. The composition of claim 30, wherein said composition is adapted for administration of said ghrelin or analog thereof
15 at a dose of about 1 µg/kg.

42. The composition of claim 30, wherein said composition is adapted for administration of said unacetylated ghrelin or analog thereof at a dose of about 1 µg/kg.

43. The method of claim 2, wherein said insulin-associated
20 parameter is selected from the group consisting of:

(a) insulin level;

(b) insulin resistance;

(c) free fatty acid level;

(d) insulin activity;

25 (e) insulin sensitivity; and

(f) any combination of (a) to (e).

44. The method of claim 43, wherein said alteration of an insulin-associated parameter is selected from the group consisting of:

- (a) a decrease in insulin level;
- 5 (b) a decrease in insulin resistance;
- (c) a decrease in free fatty acid level; and
- (d) any combination of (a) to (c).

45. The method of claim 2, wherein said method is for preventing or treating an insulin-associated condition.

10 46. The method of claim 45, wherein said insulin-associated parameter is insulin resistance.

47. The method of claim 46, wherein said insulin resistance is associated with a state or condition selected from the group consisting of:

- 15 (a) postprandial state;
- (b) reduced growth hormone level;
- (c) reduced growth hormone activity;
- (d) obesity;
- (e) diabetes;
- 20 (f) intravenous nutrition due to critical illness;
- (g) metabolic syndrome X; and
- (h) any combination of (a) to (g).

48. The method of claim 47, wherein said state or condition is reduced growth hormone level, activity, or both.

49. The method of claim 48, wherein said reduced growth hormone level, activity, or both are associated with a condition selected from the group consisting of:

(a) obesity;

5 (b) aging;

(c) pituitary gland deficiency;

(d) intravenous nutrition; and

(e) any combination of (a) to (d).

10 50. The method of claim 47, wherein said state or condition is diabetes.

51. The method of claim 50, wherein said diabetes is selected from the group consisting of type I diabetes and type II diabetes.

15 52. The method of claim 51, wherein said diabetes is type I diabetes.

53. The method of claim 52, said method is for preventing or treating the dawn phenomenon.

54. A package comprising a ghrelin or analog thereof and an unacylated ghrelin or analog thereof.

20 55. The package of claim 54, further comprising instructions for altering an insulin-associated parameter in a subject.

56. A package comprising the composition of claim 30.

25 57. The package of claim 56, said package further comprising instructions for altering an insulin-associated parameter in a subject.

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58. Use of the composition of claim 30 for the alteration of an insulin-associated parameter in a subject.

59. Use of the composition of claim 30 for the preparation of a medicament for the alteration of an insulin-associated
5 parameter in a subject.

60. Use of the composition of claim 31 for the alteration of an insulin-associated parameter in a subject.

61. The use of claim 58, wherein said insulin-associated parameter is selected from the group consisting of:

- 10 (a) insulin level;
- (b) insulin resistance;
- (c) free fatty acid level;
- (d) insulin activity;
- (e) insulin sensitivity; and
- 15 (f) any combination of (a) to (e).

62. The use of claim 61, wherein said alteration of an insulin-associated parameter is selected from the group consisting of:

- (e) a decrease in insulin level;
- 20 (f) a decrease in insulin resistance;
- (g) a decrease in free fatty acid level; and
- (h) any combination of (a) to (c).

63. The use of claim 58, wherein said alteration is for the prevention or treatment an insulin-associated condition.

64.The use of claim 62, wherein said insulin-associated parameter is insulin resistance.

65.The use of claim 64, wherein said insulin resistance is associated with a state or condition selected from the group consisting of:

- (a) postprandial state;
- (b) reduced growth hormone level;
- (c) reduced growth hormone activity;
- (d) obesity;
- (e) diabetes;
- (f) intravenous nutrition due to critical illness;
- (g) metabolic syndrome X; and
- (h) any combination of (a) to (g).

66.The use of claim 65, wherein said state or condition is reduced growth hormone level, activity, or both.

67.The use of claim 66, wherein said reduced growth hormone level, activity, or both are associated with a condition selected from the group consisting of:

- (a) obesity;
- (b) aging;
- (c) pituitary gland deficiency;
- (d) intravenous nutrition; and
- (e) any combination of (a) to (d).

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68.The use of claim 65, wherein said state or condition is diabetes.

69.The use of claim 68, wherein said diabetes is selected from the group consisting of type I diabetes and type II diabetes.

70.The use of claim 69, wherein said diabetes is type I diabetes.

71.The use of claim 70, said method is for preventing or treating the dawn phenomenon.

72.The use of claim 58, wherein said ghrelin comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 1 and a fragment thereof.

73.The use of claim 72, wherein said ghrelin comprises a peptide having the amino acid sequence of SEQ ID NO: 1.

74.The use of claim 58, wherein said unacylated ghrelin comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 2 and a fragment thereof.

75.The use of claim 74, wherein said unacylated ghrelin comprises a peptide having the amino acid sequence of SEQ ID NO: 2.

76.The use of claim 58, wherein said analog of ghrelin comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 3 and a fragment thereof.

77.The use of claim 76, wherein said analog of ghrelin comprises a peptide having the amino acid sequence of SEQ ID NO: 3.

78.The use of claim 58, wherein said analog of unacylated ghrelin comprises an amino acid sequence substantially identical to a sequence selected from the group consisting of SEQ ID NO: 4 and a fragment thereof.

79.The use of claim 78, wherein said analog of unacylated ghrelin comprises a peptide having the amino acid sequence of SEQ ID NO: 4.

80.The use of claim 58, wherein said composition is adapted for an administration by a route selected from the group consisting of intravenous, oral, transdermal, subcutaneous, mucosal, intramuscular, intranasal, intrapulmonary, parenteral, intrarectal and topical.

81.The use of claim 58, wherein said ghrelin or analog thereof is adapted for administration at a dose of about 1 µg/kg.

82.The use of claim 58, wherein said unacetylated ghrelin or analog thereof is adapted for administration in a dose of about 1 µg/kg.

83.The use of claim 58, wherein said subject is a mammal.

84.The use of claim 83, wherein said subject is human.

85.A composition comprising a ghrelin or analog thereof and an unacylated ghrelin or analog thereof for use as a medicament.

86. Use of a composition comprising a ghrelin or analog thereof and an unacylated ghrelin or analog thereof as a medicament.